

Amendments to the Claims

1.-9. (Canceled)

10. (Previously presented) A method for treating sexual arousal disorder comprising:
administering to a female subject in need thereof, an effective amount of an estrogen agonist / antagonist, and further comprising co-administering a cyclic guanosine 3',5'-monophosphate elevator.

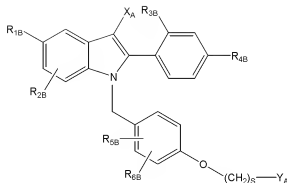
11. (Previously presented) The method of claim 10 wherein said cyclic guanosine 3',5'-monophosphate elevator is a PDE_v phosphodiesterase inhibitor.

12. (Previously presented) The method of claim 11 wherein the PDE_v phosphodiesterase inhibitor is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sulfonyl]-4-methylpiperazine citrate salt.

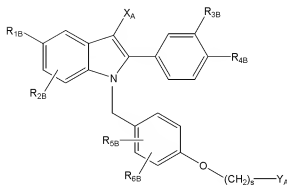
Claims 13.-39. (canceled)

40. (Currently amended) The method of claim 4 10 wherein said estrogen agonist / antagonist is selected from the group consisting of tamoxifen, 4-hydroxy tamoxifen, raloxifene, toremifene, centchroman, idoxifene, 6-(4-hydroxy-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-benzyl]-naphthalen-2-ol, [4-[2-(2-aza-bicyclo[2.2.1]hept-2-yl)-ethoxy]-phenyl]-[6-hydroxy-2-(4-hydroxy-phenyl)-benzo[b]thiophen-3-yl]-methanone, EM-652, EM-800, GW 5638, GW 7604, or ~~an optical or geometric isomer thereof~~; a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or prodrug thereof.

41. (Currently amended) The method of claim 4 10 wherein said estrogen agonist / antagonist is a compound selected from the formulas V or VI:



(V)



(VI)

wherein:

R_{1B} is selected from H, OH, $-O-C(O)-C_1-C_{12}$ alkyl (straight chain or branched), $-O-C_1-C_{12}$ alkyl (straight chain or branched or cyclic), or halogens or C_1-C_4 halogenated ethers,

R_{2B} , R_{3B} , R_{4B} , R_{5B} , and R_{6B} are independently selected from H, OH, $-O-C(O)-C_1-C_{12}$ (straight chain or branched), $-O-C_1-C_{12}$ (straight chain or branched or cyclic), halogens, or C_1-C_4 halogenated ethers, cyano, C_1-C_6 alkyl (straight chain or branched), or trifluoromethyl, with the proviso that, when R_{1B} is H, R_{2B} is not OH;

X_A is selected from H, C_1-C_6 alkyl, cyano, nitro, trifluoromethyl, and halogen;

s is 2 or 3;

Y_A is the moiety:



wherein:

a) R_{7B} and R_{8B} are independently selected from the group of H, C₁-C₆ alkyl, or phenyl optionally substituted by CN, C₁-C₆ alkyl (straight chain or branched), C₁-C₆ alkoxy (straight chain or branched), halogen, -OH, -CF₃, or -OCF₃; or

b) R_{7B} and R_{8B} are concatenated to form a five-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfanyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or

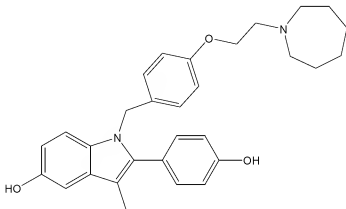
c) R_{7B} and R_{8B} are concatenated to form a six-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfanyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or

d) R_{7B} and R_{8B} are concatenated to form a seven-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfanyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or

e) R_{7B} and R_{8B} are concatenated to form an eight-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfanyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄)alkyl; or

f) R_{7B} and R_{8B} are concatenated to form a saturated bicyclic heterocycle containing from 6-12 carbon atoms either bridged or fused and containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C₁-C₄ alkyl, trihalomethyl, C₁-C₄ alkoxy, trihalomethoxy, C₁-C₄ acyloxy, C₁-C₄ alkylthio, C₁-C₄ alkylsulfanyl, C₁-C₄ alkylsulfonyl, hydroxy (C₁-C₄)alkyl, -CO₂H, -CN, -CONHR_{1B}, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)₂, -NHSO₂R_{1B}, -NHCOR_{1B}, -NO₂, or phenyl optionally substituted with 1-3 (C₁-C₄) alkyl; ~~or an optical or geometric isomer thereof;~~ or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

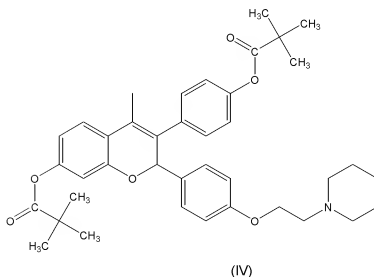
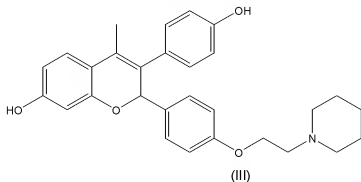
42. (Previously presented) The method of claim 41 wherein said estrogen agonist / antagonist is the compound, TSE-424, of formula Va below:



(Va)

or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

43. (Currently amended) The method of claim 4 10 wherein said estrogen agonist / antagonist is EM-652 of formula III below or is EM-800 of formula IV below:



or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

44. – 45. (Canceled)

46. (Currently amended) A method for treating sexual arousal disorder comprising: administering to a female subject in need thereof, an effective amount of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol or ~~an optical or geometric isomer thereof~~; a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof and further comprising co-

administering an effective amount of a cyclic guanosine 3',5'-monophosphate elevator.

47. (Previously presented) The method of claim 46 wherein the cyclic guanosine 3',5'-monophosphate elevator is a PDE_v phosphodiesterase inhibitor.

48. (Previously presented) The method of claim 47 wherein the PDE_v phosphodiesterase inhibitor is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sulfonyl]-4-methylpiperazine citrate salt.

49. (canceled)

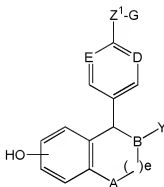
50. (Currently amended) The method of claim ~~46, 47 or 48 wherein (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol, D-tartrate salt is administered~~ 45 wherein the female subject is postmenopausal.

51. (Currently amended) The method of claim ~~45~~ 48 wherein the female subject is pre-menopausal.

52. (Previously presented) The method of claim 46 wherein the female subject is postmenopausal.

53. (Previously presented) The method of claim 46 wherein the female subject is pre-menopausal.

54. (new) The method of claim 10 wherein the estrogen agonist/antagonist is a compound of formula (I):



(I)

wherein:

A is selected from CH_2 and NR ;

B, D and E are independently selected from CH and N;

Y is

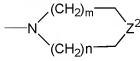
- (a) phenyl, optionally substituted with 1-3 substituents independently selected from R^4 ;
- (b) naphthyl, optionally substituted with 1-3 substituents independently selected from R^4 ;
- (c) $\text{C}_3\text{-C}_8$ cycloalkyl, optionally substituted with 1-2 substituents independently selected from R^4 ;
- (d) $\text{C}_3\text{-C}_8$ cycloalkenyl, optionally substituted with 1-2 substituents independently selected from R^4 ;
- (e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of $-\text{O}-$, $-\text{NR}^2-$ and $-\text{S}(\text{O})_n-$, optionally substituted with 1-3 substituents independently selected from R^4 ;
- (f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of $-\text{O}-$, $-\text{NR}^2-$ and $-\text{S}(\text{O})_n-$ optionally substituted with 1-3 substituents independently selected from R^4 ; or
- (g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of $-\text{O}-$, $-\text{NR}^2-$ and $-\text{S}(\text{O})_n-$, optionally substituted with 1-3 substituents independently selected from R^4 ;

Z^1 is

- (a) $-(\text{CH}_2)_p \text{W}(\text{CH}_2)_q-$;

- (b) $-\text{O}(\text{CH}_2)_p \text{CR}^5\text{R}^6-$;
- (c) $-\text{O}(\text{CH}_2)_p \text{W}(\text{CH}_2)_q-$;
- (d) $-\text{OCHR}^2\text{CHR}^3-$; or
- (e) $-\text{SCHR}^2\text{CHR}^3-$;

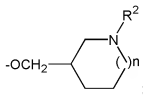
G is

- (a) $-\text{NR}^7\text{R}^8-$;
- (b) 

wherein n is 0, 1 or 2; m is 1, 2 or 3; Z² is -NH-, -O-, -S-, or -CH₂-;


optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from R⁴; or

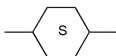
(c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R⁴; or



Z¹ and G in combination may be

W is

- (a) $-\text{CH}_2-$;
- (b) $-\text{CH}=\text{CH}-$;
- (c) $-\text{O}-$;
- (d) $-\text{NR}^2-$;
- (e) $-\text{S}(\text{O})_n-$;
- (f) ;
- (g) $-\text{CR}^2(\text{OH})-$;
- (h) $-\text{CONR}^2-$;
- (i) $-\text{NR}^2\text{CO}-$;



(j) ; or

(k) $-C\equiv C-$;

R is hydrogen or C_1-C_6 alkyl;

R^2 and R^3 are independently

(a) hydrogen; or

(b) C_1-C_4 alkyl;

R^4 is

(a) hydrogen;

(b) halogen;

(c) C_1-C_6 alkyl;

(d) C_1-C_4 alkoxy;

(e) C_1-C_4 acyloxy;

(f) C_1-C_4 alkylthio;

(g) C_1-C_4 alkylsulfinyl;

(h) C_1-C_4 alkylsulfonyl;

(i) hydroxy (C_1-C_2)alkyl;

(j) aryl (C_1-C_4)alkyl;

(k) $-CO_2H$;

(l) $-CN$;

(m) $-CONHOR$;

(n) $-SO_2NHR$;

(o) $-NH_2$;

(p) C_1-C_4 alkylamino;

(q) C_1-C_4 dialkylamino;

(r) $-NHSO_2R$;

(s) $-NO_2$;

(t) $-aryl$; or

(u) $-OH$;

R^5 and R^6 are independently C_1-C_8 alkyl or together form a C_3-C_{10} carbocyclic

ring;

R^7 and R^8 are independently

(a) phenyl;

- (b) a C₃-C₁₀ carbocyclic ring, saturated or unsaturated;
- (c) a C₃-C₁₀ heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;
- (d) H;
- (e) C₁-C₆ alkyl; or
- (f) form a 3 to 8 membered nitrogen containing ring with R⁵ or R⁶;

R⁷ and R⁸ in either linear or ring form may optionally be substituted with up to three substituents independently selected from C₁-C₆ alkyl, halogen, alkoxy, hydroxy and carboxy;

a ring formed by R⁷ and R⁸ may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

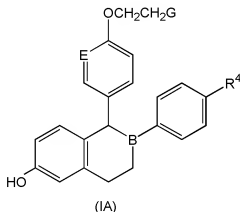
n is 0, 1 or 2;

p is 0, 1, 2 or 3;

q is 0, 1, 2 or 3;

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

55. (new) The method of claim 54 wherein said estrogen agonist / antagonist is a compound of formula (IA):



wherein G is



R^4 is H, OH, F, or Cl; and B and E are independently selected from CH and N or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.